

**Name of Journal:** *World Journal of Gastrointestinal Oncology*

**Manuscript NO:** 64595

**Manuscript Type:** REVIEW

**Title:** B7 homologue 3 as a prognostic biomarker and potential therapeutic target in gastrointestinal tumors

**Authors:** Petar Rasic, Maja Jovanovic-Tucovic, Marija Jeremic, Slavisa M Djuricic, Zorica V Vasiljevic, Maja Milickovic, Djordje Savic

**Corresponding author: Petar Rasic, MD,** Department of Abdominal Surgery, Mother and Child Health Care Institute of Serbia “Dr. Vukan Cupic,“ Radoja Dakica 6-8, Belgrade 11 000, Serbia. petar.rasic@imd.org.rs

Dear Editors and Reviewers,

We highly appreciate the effort and time you devoted to evaluating this manuscript. We have read your insightful comments and have revised the manuscript.

All of the revisions are highlighted in yellow in the updated version of the manuscript.

We respond below to your comments item-by-item.

**Response to Editorial comments:**

**COMMENT 1:** The authors did not provide the approved grant application form(s). Please upload the approved grant application form(s) or funding agency copy of any approval document(s)

**Response:** We prefer to delete part „Supported by“.

**COMMENT 2:** The authors did not provide original pictures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor.

**Response:** We prepared and arranged the figure in PowerPoint, and the original figure document is submitted now with other accompanying documents.

**COMMENT 3:** The “Article Highlights” section is missing. Please add the “Article Highlights” section at the end of the main text.

**Response:** According to the instructions written in the e-mail we have received from Company Editor-in-Chief, our manuscript, being categorized as a „Review“, does not need to contain “Article highlights”: *Requirements for article highlights: If your manuscript is an original study (basic study or clinical study), meta-analysis, or systemic review, the “Article Highlights” section should be provided.*

*Detailed writing requirements for “Article Highlights” can be found in the Guidelines and Requirements for Manuscript Revision.*

We had written to the Editorial office regarding this dilemma and obtained additional instruction from Science Editor that we do not need to add the “Article Highlights” section into the manuscript.

**COMMENT 4:** If an author of a submission is re-using a figure or figures published elsewhere, or that is copyrighted, the author must provide documentation that the previous publisher or copyright holder has given permission for the figure to be re-published; and correctly indicating the reference source and copyrights.

**Response:** The figure we used in this manuscript is our original figure. The figure is not published elsewhere, and it is not copyrighted.

**COMMENT 5:** Please resolve all language issues in the manuscript based on the peer review report. Please be sure to have a native-English speaker edit the manuscript for grammar, sentence structure, word usage, spelling, capitalization, punctuation, format, and general readability, so that the manuscript’s language will meet our direct publishing needs.

**Response:** We have resolved all the language issues in the manuscript. A native English speaker edited the manuscript. The text is now more streamlined, and sentence structure and general readability are improved.

#### **Responses to Reviewer #02897448’s comments**

**COMMENT 1:** Regarding the description of the research progress of B3-H7 in esophageal cancer, compared with colorectal cancer and gastric cancer, the authors did not have a good integration, classification and summary of previous studies. For example, colorectal cancer and gastric cancer are divided into four sections to review previous studies, but the esophageal cancer section was not organized well.

**Response:** We have reorganized the „Esophageal cancer“ section, and now it consists of two sections: *B7-H3 in tumor cells of esophageal cancer and immunity*, and *B7-H3 promotes progression in esophageal cancer*. In contrast to colorectal cancer and gastric cancer, unfortunately, there are just a few published studies regarding B7-H3 involvement in the pathogenesis of esophageal cancer (references numbers: 26, 127, 132, and 137). Although the published studies reveal the association of B7-H3 with immune cell infiltration, and tumor cell invasion, migration, and proliferation, none of them explains the precise molecular mechanisms of B7-H3 role in the progression of esophageal cancer (*e.g.*, the specific signaling pathway activation). Consequently, the sections are less detailed comparing to those regarding colorectal and gastric cancer. Besides, there are no studies regarding potential B7-H3 antiapoptotic activity in esophageal cancer or its influence on cancer cell metabolism of this tumor. Therefore, it was impossible to create sections such as *B7-H3 antiapoptotic activity in esophageal cancer* and *B7-H3 role in esophageal cancer cell metabolism*.

**COMMENT 2:** Regarding the mechanism of action of B3-H7 in various gastrointestinal cancers and their cells, it is recommended that the authors make a graphical summary. It would be better if the authors draw a schematic diagram of the mechanism.

**Response:** Figure 1 represents the schematic graphical summary of the mechanisms of action of B7-H3 in gastrointestinal cancers.

**Responses to Reviewer #05402068's comments**

Thanks for your comment.

**ADDITIONAL MINOR CHANGES:** Also, several minor improvements were made in the manuscript.

We thank the Editors and Reviewers for their helpful comments and suggestions to improve our manuscript, and we look forward to your response.

Please do not hesitate to contact us with any additional questions or concerns.

Best regards,

Petar Rasic